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Melanotic Schwannoma of the Cervical Spine Progressing With Pulmonary Metastasis: Case Report

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Abstract

Melanotic schwannoma (MS) is an unusual variant of nerve sheath neoplasm. Only 10% of these tumors will undergo malignant degeneration, with exceedingly rare reported metastasis. We present a 32-year-old woman with a 6-month history of cervical pain and left arm progressive weakness. Neurological examination showed a left upper limb radicular pain, with pyramidal syndrome at C5 level. The magnetic resonance imaging (MRI) study highlighted an intradural extramedullary heterogeneous mass along the spinal cord at the C4–C5 level, slightly hyperintense with T_1 and hypointense with T_2-weighted sequences, invading the left neural foramen. The patient underwent C3–C5 laminectomy with total resection of a black tumor. In the postoperative period, a patent deficit of shoulder abduction ensued related to the nervous section. Microscopically, compactly fascicles of spindle-shaped cells with pleomorphic and hypercromatic nuclei, dark brown intracellular pigments, as well as some mitotic figures were seen. Immunohistochemical stains for S-100, Human Melanoma Black-45 (HMB-45), and vimentin were positive, with Ki-67 labelling index (LI) of 15% compatible with MS. Six months after radiotherapy she presents local recurrence and lung metastatic dissemination of the MS. She underwent left pulmonary segmentectomy, followed by chemotherapy and radiosurgery. The patient developed a febrile neutropenia and worsening of general status, and died after 3 months due to respiratory complications. MS are rare tumors with potential for local recurrence and distal metastasis. Complete surgical resection remains as the treatment of choice, once the uncommon cases with malignant progression shows low response to chemo and radiotherapy.

Key words: cervical neoplasm, melanotic schwannoma, metastasis, nerve sheath tumor, spine

Introduction

Melanotic neoplasm of the central nervous system (CNS) are rare, and most frequently they are metastatic.[13,16] It is important to differentiate primary melanin-containing lesions of the CNS from metastatic melanomas, because these last tumors require a specific therapeutic approach. Other pigmented lesions include neoplasms that may undergo melanization, such as schwannoma, medulloblastoma, and glioma, as well as melanocytic neuroectodermal tumors of infancy.[1,11,13,20]

Melanotic schwannoma (MS) is an unusual variant of nerve sheath neoplasm composed of cells having the ultrastructure and immunophenotype of Schwann cells but containing melanosomes in varying stages of maturation.[5] These tumors were first described by Hodson in 1961, with only about 100 cases reported in the literature until now.[4] Two forms of MS are described: psamomatous and sporadic. Psamomatous type occurs in the setting of the autosomal dominant Carney complex, a multiple neoplasia syndrome characterized by a markedly increased risk to develop myxomas (cardiac, mammary, and cutaneous), mucocutaneous lentigines and blue nevi, and functional endocrine tumors (cushing syndrome, precocious puberty, and acromegaly).[15,18] Nearly two-thirds of patients with Carney complex have mutations spread over the PRKAR1A gene, which encodes the R1a regulatory subunit of cyclic-adenosine monophosphate-activated protein kinase (cAMP)-dependent protein kinase A.[6,10] Psamomatous tumors typically occur in patients a decade younger than sporadic cases, which peak prevalence in the fourth decade of life. Patients who develop tumors

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at an earlier age may be more likely to have Carney's syndrome.[11,19]

MSs are more typically intracranial, but they also occur within the spinal canal. When they develop within spine, the tumors most often arise in the lombo-sacral region (47.2%) followed by thoracic (30.5%) and cervical (22.2%) levels, and may be intramedullary.[12] The behavior of these tumors is typically benign, but 10% of MS will undergo malignant degeneration. Metastasis and meningeal seeding have been reported but are exceedingly rare.[17] Killeen et al. found a recurrence rate of 24% and a disease-related mortality of 16%, with complete surgical excision being the most common initial treatment.[9]

Case Report

A 32-year-old woman had a 6-month history of cervical pain and left arm progressive weakness. On admission, neurological examination showed a left upper limb radicular pain, with pyramidal syndrome and paresthesic area at C5 level. The magnetic resonance imaging (MRI) study highlighted an intradural extramedullary heterogeneous mass along the spinal cord at the C4–C5 level, slightly hyperintense with T_1 and isointense with T_2-weighted sequences, invading the left C5 neural foramen (Fig. 1). The patient underwent C3–C5 laminectomy with total resection of a black encapsulated tumor measuring 37 × 30 × 16 mm (Fig. 2). In the postoperative period, a patent deficit of left shoulder abduction and paresthesia persist related to the nervous section. The search for clinical signs of melanoma, neurofibromatosis, or Carney's syndrome was negative. Microscopically, compact fascicles of epithelioid and spindle-shaped cells with pleomorphic and hypercromatic nuclei and dark brown intracellular pigment as well as some mitotic figures were seen. Several foci of necrosis and macrophage with large brown cytoplasmic granule were also visible. Immunohistochemical stains for S-100, Human Melanoma Black-45 (HMB-45) and vimentin were positive, with Ki-67 labelling index (LI) of 15%, compatible with MS (Fig. 3). She was submitted to external radiotherapy (40 Gy) and remains clinically stable. Six months later, she presents worsening of cervical pain and dyspnoea, with evidence of local recurrence

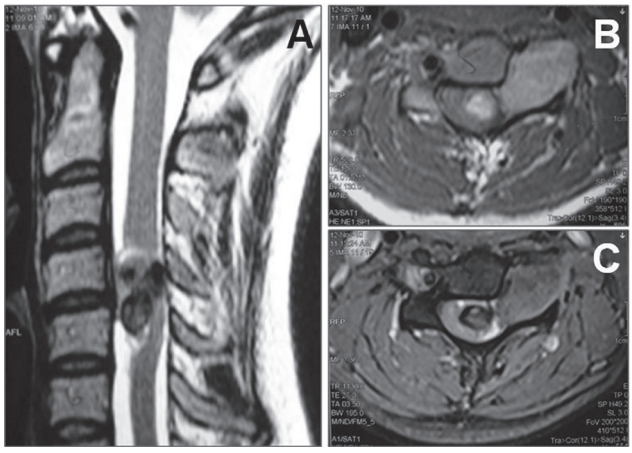

Fig. 1 A: MRI study with sagittal T_2-weighted sequence disclosing a hypointense heterogeneous intradural C4–C5 mass, disrupting the medulla. B: axial T_2 proton density (PD)-weighted sequence showing a slightly hyperintense. C: Axial FLAIR isointense extramedullary neoplasm extension for the left C5 root without bone destruction, presenting an hourglass shape directed toward the paravertebral area. FLAIR: fluid attenuated inversion recovery, MRI: magnetic resonance imaging.

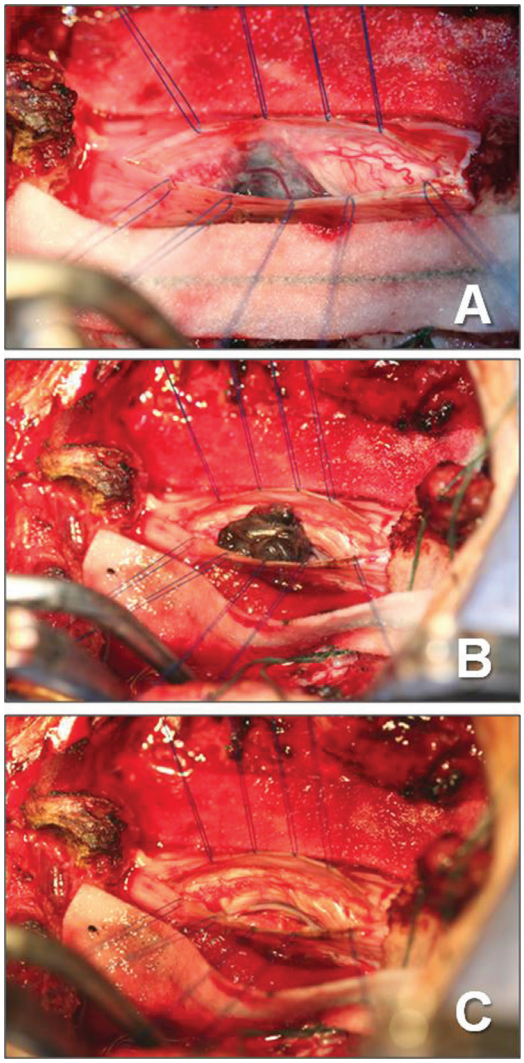

Fig. 2 Surgical view of C3–C5 laminectomy followed by durotomy, revealing (A) intradural extramedullary mass, with (B) black multilobulated appearance that extended to C5 foramen, as confirmed after (C) the total removal of tumor.

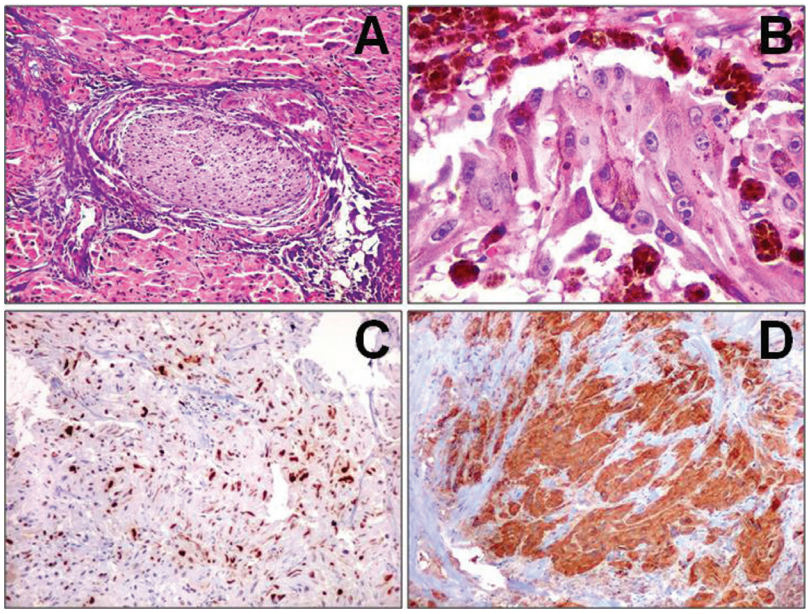

Fig. 3 Microscopic view of melanotic schwannoma (MS) showing A: a neoplasm with markedly pleomorphic and variable dark brown pigmented Schwann cells with hyperchromatic nuclei surrounding a small nerve root [H&E; ×200], B: a detail of spindle-shaped neoplastic epithelioid cells and activated macrophages with melanin granules [H&E; ×1000], C: a immunostain for Ki-67 displaying the tumor proliferative status (LI = 15%) [H&E; ×200], D: a strong positivity for melanoma-associated antigen HMB-45 [H&E; ×200]. H&E: Harry's hematoxylin, LI: labelling index.

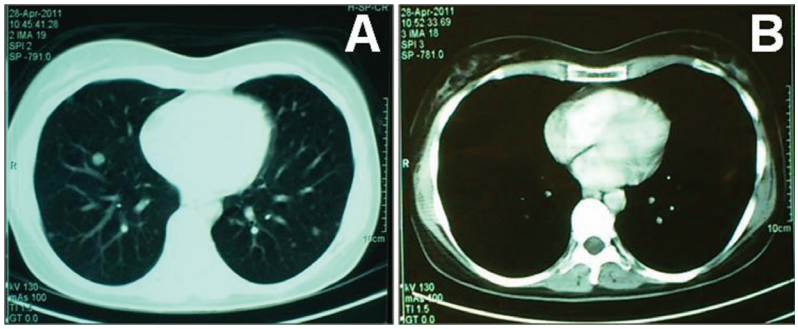

Fig. 4 Computed tomography (CT) scan of the chest showing multiple pulmonary nodules scattered throughout both lungs with thin post contrast enhancing, measuring from a few millimeters to 2 cm. No adenopathy is seen in either the hilar region or the rest of the mediastinum. A: lung filter, B: osseous filter.

and multiple pulmonary nodules (Fig. 4). She was started on multiagent chemotherapy (dicarbazine, cisplatin, and interferon) and submitted to cervical stereotactic radiosurgery (800 cGy). The patient also underwent left pulmonary segmentectomy, which confirmed the metastatic dissemination of the MS. She evolved with progressive deterioration of general status and pleural effusion, being diagnosed a febrile neutropenia. The patient died after 3 months due to respiratory/infectious complications.

Discussion

Primary pigmented tumors of the nervous system are rare. MS generally arise from the roots of spinal nerves, or occasionally from soft tissues. A number of cases were reported in the bone, sympathetic chain, cerebellar, heart, liver, choroids, and skin. Intramedullary, these tumors seems to appear more frequently in the lombosacral region and less commonly in the cervical spine. Moreover, most previously reported cases behaved in a clinically benign fashion.[2,3,8,12]

MS presents a 1.1:1 male-female ratio, age at diagnosis varying from 10 to 84 years, with the highest frequency of occurrence in the fourth decade. Patients who develop tumors at an earlier age (third decade) may be more likely to have Carney's syndrome which is associated up to 50% of cases of these lesions.[15] For this, it is necessary to search for clinicopathologic components of Carney's complex.[18] The patient described herein had no evidence of genetic syndromes, including neurofibromatosis, consisting probably in an example of a sporadic case of MS.[11]

In these neoplasms, the common radiological features include a hyperintense signal on the T_1-weighted images related to the considerable amount of melanin, whereas ordinary schwannomas give isosignals on T_1-weighted images. The MRI study reveals early erosion of the intervertebral foramen with an "hourglass" extension and isointense to slightly hyperintense signal in the T_2-weighted images. However, their signal characteristics vary, and areas of T_1 and T_2 prolongation may be seen.

On post contrast images, the enhancement pattern of the lesions also varies.[2,16]

The histological findings of the present case are similar to those sporadic MS reported previously, consisting of spindle cells packed in interlacing fascicles. Mitoses, cellular atypia, increased cellularity, and infiltrating ill-defined borders are described as signs of malignancy in nerve-sheath tumors.[5,13] The differential diagnosis between MS and other pigmented lesions can be difficult, including primary or metastatic melanoma, a diagnosis with obvious prognostic and therapeutic relevance. In addition, these tumors may histologically closely resemble leptomeningeal melanocytomas and cellular blue nevi.[8,12]

Several theories for the etiology of MS have been proposed, including the melanomatous transformation of neoplastic Schwann cells, phagocytosis of melanin by Schwann cells, and the simultaneous presence of two distinct neoplastic populations of proliferating melanocytes and Schwann cells.[14] However, it is actually accepted that Schwann cells, melanoblasts, and melanocytes are of neuroectodermal origin and also that melanocytes appear to migrate with Schwann cells.[13] So, we hypothesize that some genetic alterations in a common precursor may trigger the tumorigenic process, making these proliferating cells with schwannian phenotype to synthesize melanin, leading finally to the development of MS.

Immunostaining analyses are important, but not always useful in sorting out this differential diagnosis. All these lesions generally express S-100, which can be explained by their common neural crest origin. Melanocytic differentiation can be expressed by HMB-45 and Melan-A positivity, which recognizes melanosomal components in tumor cells.[21] Although stains for components of the basement membrane can be useful in discriminating tumors with schwannian differentiation from tumors with melanocytic differentiation, overlap in staining patterns has been noted.[7]

Surgery is universally accepted as the best form of treatment. Radical surgical excision with wide range margins and without regional lymph-nodes dissection remains the technique of choice, as lymph-node involvement is extremely rare. Incomplete tumor removal is associated with recurrence risk. As for other sarcomas, the role of postoperative radiation therapy and/or chemotherapy is not yet well defined.[3,5,11] In recent studies, postoperative radiation therapy is also recommended to reduce the possibility of local recurrence. Chemotherapy has been advocated for patients with unresectable recurrent tumor or distant metastases. The role in survival of adjuvant therapies has yet to be defined.[13,16]

Advanced age seems to be a factor of poor prognosis in sporadic forms; indeed, metastatic recurrence occurs among populations aged less than 40 years. No other prognosis factors such immunohistochemical stains or efficiency of chemotherapy or radiotherapy protocols has been reported in the literature.[9,17]

Thereafter, the multiple pulmonary lesions diagnosed on patient's clinical course showed exactly the same histological configuration as the initial cervical lesions, including the pigmented macroscopic appearance and the immunohistochemical findings, reinforcing the causal and temporal relationship between these lesions. Though this type of tumor may arise from peripheral nerves located within the bronchial wall, primary endobronchial schwannomas are extremely rare, with incidence estimated in 0.2% of all lung tumors, presenting usually as a single nodule or mass.[11,21]

Thus, the current case presented an unusual malignant progression, with pulmonary metastasis. Multiple MS of the nerve sheath and/or heterotypic sites are possible and have been commonly thought to be synchronous or metachronous tumors of different origins rather than metastatic foci.[12,19] Moreover, as in some previous reports, the complete macroscopical removal of the main lesion does not guarantee recovery which would be free of local recurrence and future metastasis.[2,11,16]

Conclusion

MS is a rare neoplasm composed of Schwann cells capable of melanogenesis, which maybe encountered by spine surgeons involving cervical nerve trunks. These tumors are usually benign, but they may become aggressive and metastasize. Total excision with tumor-free margins and a long-term follow-up is recommended, including the screening for Carney's syndrome especially in young patients.

Conflicts of Interest Disclosure

None declared.

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